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Review Article

Terrifying Aspects of Gene Mutation: A Review

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Abstract: Mutation refers to alteration of DNA sequence, which may occur either naturally or artificially by various physical, chemical or biological agents. There are many conventional (Replica plating, antibiotic enrichment, use of chromogenic substrates and Ames test) and modern techniques (Denaturing HPLC, TILLING, PCR, NGS, gene probes, southern blotting, DNA sequencing, DNA microarray) for the identification of mutants. Some of the mutations are beneficial, while others may show deleterious effects. There are many beneficial approaches of mutagenesis in various fields ranging from biomedical applications to crop improvement. In biomedical sector, this approach is used for developing vaccines, somatic and germ line gene therapy and treating various diseases through knockout technology. Many improved strains of crops like rice, maize, cotton, tomato and potato have been developed using mutagenesis approach either by silencing of genes or overproduction of product through mutagenic approach. Various improved fermented food products have also been produced by developing improved microbial strains with enhanced and better quality product formation. Along with biomedical and food sector, this approach is also used in the environmental sector for developing microbial strains showing resistance towards environmental stress. Such microbial strains can be easily utilized in bioremediation for degrading xenobiotics, which cause environmental pollution. However, mutagenesis not always shows beneficial aspects, it may also result in deleterious consequences resulting in allergies and other side effects. There is need to conduct preclinical studies on animals and mammalian cell lines before commercialization of product or therapy involving mutagenesis. Therefore, the focus of current study is to understand the beneficial and deleterious effects of mutagenesis.
Keywords: Mutation, beneficial, deleterious, PCR, NGS, therapy, xenobiotic, allergy

INTRODUCTION

Mutation is alteration in the nucleotide sequence of DNA compared to wild type sequence, which may or may not affect the phenotype of organism [1]. The term mutation was derived from Latin word meaning “to change” and it was given by Hugo de Vries [2]. Mutations may occur spontaneously due to variation, which play an important role in evolution or it may induce artificially by various mutagens [3]. Induced mutations may result by the action of certain physical (ionizing and non-ionizing radiations), chemical (5-Bromouracil, chelating dyes) or biological (viruses) agents. The common mechanisms during the mutation are insertion, deletion or substitution of a nucleotide [4]. The alteration in genes during this process may have beneficial or deleterious influences in the characteristics of an organism. The present review will focus on conventional and modern methods for the identification of mutants. Thereafter, beneficial and deleterious aspects of induced mutations will also be discussed.

Techniques for Identification of Mutants

Replica plating, antibiotic enrichment, use of chromogenic substrates and Ames test are some of the conventional techniques used for the identification of mutants [5-7]. Denaturing HPLC (High Performance Liquid Chromatography) and TILLING (Targeting Induced Local Lesions in Genome) techniques are used for the selection of mutant strains from wild strains [8].

The modern techniques, which are used for the identification of mutants are gel electrophoresis, polymerase chain reaction (PCR), gene probes, southern blotting[3], DNA sequencing, next generation sequencing (NGS)[9] and DNA microarray [10,11].

Beneficial Effects of Mutation

Bacteria act as model organism for the detection of beneficial or harmful effects of mutation by introducing genetic variation into the growing population through different mechanisms. The selection of bacteria is due to its unique features like rapid reproduction, large population size, easy to handle and rapid adaptation for a variety of environmental changes [12]. There are many previous reports published by various authors on beneficial mutations. The increased fitness of *Escherichia coli* to the cultivation condition due to disruption of genetic activity created by knockout mutations has been reported by Lenski *et al.;* in 1998 [13]. The regulatory control of *spo*T resulted in increased growth rate of mutants [14]. The adaptive mutations due to environmental responses like presence of synthetic compounds (nylon, toluene, phenol), nutrient starvation, temperature stress, salt stress etc. result in development of mutant strains with enhanced gene and enzyme expression, increased survival under extreme or stressful conditions and degradation of various xenobiotic compounds, an environmental friendly approach [15,16]. Mutagenesis is emerging as a promising approach for crop improvement [8]. Alteration of genes using recombinant DNA technology is currently used for developing genetically modified animals and crops. Genetically engineered models possess many advantages for preclinical studies over xenografts [17]. Many genetically modified crops have been developed and their preclinical studies have also been conducted before marketing to ensure safety levels of such crops [18]. Increased resistance to toxicity and oxidative stress has been observed in *Caenorhabditis elegans* when exposed to low levels of toxic agents through germline to soma communication [19].

Deleterious Effects of Mutation

Adaptive mutations have not only beneficial effects; they may also cause some of the deleterious effects, which may be lethal. Hall (1995) stated that the adaptive mutations which are useful in single cell organisms may be deleterious in multicellular organisms due to their complexity [20]. The radiation sensitivity of female germ cells in relation to folliculogenesis has been reported by Adriaens *et al.;* in 2009 [21].

Chronic and subchronic toxicity has been observed in mammals fed with commercialized genetically modified maize and soyabean [18]. Mc1r variants showed UV-induced melanoma in the animal models [22]. There are many ethical and legislation issues associated with germ line gene therapy in mammals and associated with risks to future generations [23].

CONCLUSION

Mutation is variation in the genes and it is an important approach in evolution for developing new species and strains. Mutation may occur naturally or it may induce artificially in the organisms for altering the nucleotide sequence of DNA. Many conventional and modern techniques are used to understand the effect of different mutagens and for the selection of mutagenic strains. Currently modern techniques using molecular approaches are more recommended compared to previous classical techniques due to their increased sensitivity and specificity. The mutagenesis approach has both beneficial and deleterious effects. There are many beneficial effects of mutation in biomedical, food, environment sectors. However, adaptive mutations not only result in beneficial effects, various deleterious effects have also been observed which may also be lethal due to toxicity or other side effects. Therefore, for better understanding and efficiency, mechanistic studies on animal models are required. Several current approaches like transcriptomics, proteomics and system biology can further help to understand the influence of different mutations in complex mammalian system. The safe use of mutagenic approach should also be tested to enhance public assurance.

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